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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,275	08/01/2005	Wei-Ping Min	4767-217 LAB	9949

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	
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01/21/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,275	MIN ET AL.	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/16/09, 10/07/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-61* is/are pending in the application.

4a) Of the above claim(s) *1-21,23,25,26,32-46,50 and 54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,24,27-31,47-49,51-53 and 55-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/26/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 10/07/2009 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 10/16/2008 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 10/07/2009, claims 1-61 are pending in the application. Claims 22, 24, 27-31, 47-49, 51-53 and 55-61 are currently under examination. Claims 1-21, 23, 25-26, 32-46, 50 and 54 are withdrawn as being drawn to a non-elected invention

Information Disclosure Statement

The submission of the Information Disclosure Statement on 08/26/2009 is in compliance with 37 CFR 19.7. The information disclosure statement has been considered by the examiner and signed copies have been placed in the file.

New Claim Rejection - necessitated by claim amendments

The claim amendments filed 04/16/2009 necessitates a new claim rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 recites the limitation "antigen presenting cell". There is insufficient antecedent basis for this limitation in the claim.

Claim 30 recites the limitation "immune cell". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 22, 24, 27-31, 47-49, 51-53 and 55-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Qian et al. (US 2004/0043483 of record), Li et al. (Journal of Immunology 2001, Vol. 166: pages 5619-5628 of record) and Tuschl et al. (WO 02/44321 cited on PTO 892 mailed 05/21/2007).

The instant claims are drawn to a method for treatment of an immune disorder and rejection potential of an organ for transplantation, said method comprising perfusing into said organ or administering to a mammal at least one construct that suppresses T cell activity, wherein said construct inhibits the expression of IL-12 produced in an antigen presenting cell, wherein the construct is a siRNA and wherein the antigen presenting cells are dendritic cells.

For purposes of applying art, the method of administering a composition comprising a construct would encompass administering cells comprising said construct as discussed below. Additionally, t he instant specification does not define "perfusing said organ" and therefore for purposes of prior art 'perfusing' is interpreted to mean the composition is administered through or over the organ such as by any route.

Qian et al. teach a method of preventing or minimizing transplant rejections or autoimmune diseases comprising genetically engineering dendritic cells with constructs comprising antisense compounds, ribozymes or gene silencing methods encoding endogenous genes such as IL-12, wherein the constructs may be introduced into the cells by vectors (see page 6, particularly paragraphs 0091-0094). Qian et al. teach compositions of said cells along with a pharmaceutically acceptable carrier for administration to a subject that can be administered by conventional routes such as intramuscular, intra-atrial, intraperitoneal or intravenous (see paragraphs 0096-0102).

Li et al. teach the cytokine IL-12, which is produced from antigen presenting cells such as dendritic cells, plays a key role in the regulation of autoimmune responses. Li et al. teach neutralization of IL-12 activity effectively reversed acute liver graft rejection

(see page 5625 and Figure 2). Li et al. teach decreasing the activity of IL-12 produced from dendritic cells promotes T cell apoptosis, which would be considered suppressing T cell activity that is responsible for rejection of organs and tissue (see page 5626).

Qian et al. and Li et al. do not specifically teach siRNA.

Tuschl et al. teach siRNA molecules and teach compositions comprising siRNA and an acceptable carrier that are capable of silencing gene expression (see page 9, lines 17-25). Tuschl et al. teach siRNA molecules can be designed to target any gene and can be made in expression constructs and vectors that are capable of being delivered to any cell (see page 7). Tuschl et al. teach that siRNAs represent a new alternative to previous therapeutics using inhibitory molecules.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to introduce a construct targeted to IL-12 wherein the gene silencing method is siRNA to alter T-cell activity and prevent or minimize transplant rejections or autoimmune diseases as taught by Qian et al.

One of ordinary skill in the art would have wanted to target IL-12 in methods of treatment that prevent transplant rejection and inhibit the inflammatory responses of IL-12 in autoimmune diseases as taught by Qian et al. Because it is well known to the skilled artisan that host T-cell activity is detrimental to the survival of transplanted organs and tissues and given that Li et al. teach IL-12 plays key role in the regulation of alloimmune responses and inhibiting the activity of IL-12 promotes T cell apoptosis, one would have wanted to use dendritic cells that have oligonucleotides that inhibit the

expression and activity of IL-12 in a treatment to promote the survival of transplanted organs and tissues.

In choosing an inhibitory oligonucleotide, one would have wanted to make and use a siRNA targeted to an IL-2 cytokine gene because it was well known at the time the invention was made that siRNA molecules are efficient molecules to target and decrease expression of a target gene and because the use of siRNA to inhibit gene expression is effectively more sequence specific than using other inhibitory compounds such as antisense molecules and RNAi using dsRNA is a more potent method requiring only a few molecules of dsRNA per cell. One of ordinary skill in the art would have wanted to make the siRNA to possess specific homology to the entire exon region of a gene encoding IL-12 and it would have been a matter of routine experimentation to design such a molecule in order to efficiently target the expression of IL-12. One would have been motivated to create such compounds with increased functionality, and since siRNAs are taught by Tuschl et al. as being useful in silencing gene expression, one would have looked to Tuschl et al. as a guide to design a siRNA targeted to IL-12.

One would have a reasonable expectation of success given that Tuschl et al. teach how to make and use virtually any siRNA to any gene provided the target sequence is known and teach that methods of RNA synthesis are known in the art, as evidenced by the examples provided therein and one would have expected to be able use a dendritic cell comprising an siRNA in the methods of treatment of an immune disorder as shown by Robbins et al.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicant's Arguments

Re: Claim Rejections - 35 USC § 103

The rejection of claims 22, 24, 27, 47-49, 51-53 and 55-61 under 35 U.S.C. 103(a) as being unpatentable over Robbins et al. (US Patent No. 6,936,468), Li et al. (Journal of Immunology 2001, Vol. 166: pages 5619-5628), Hammond et al. (Nature Reviews Genetics February, 2001 cited on PTO 892 mailed 05/21/2007) and Tuschl et al. (WO 02/44321 cited on PTO 892 mailed 05/21/2007) is withdrawn.

Applicant's arguments filed 4/6/2009 have been fully considered but will not be responded to given the rejection is withdrawn.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact Tracy Vivlemore at 571-272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Primary Examiner
Art Unit 1635